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Chronic endometritis: an hidden pathology

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Introduction

Chronic endometritis is a chronic inflammatory condition of the endometrium characterized by the presence of plasma cells in the endometrial stroma.[1,2] The alterations of the endometrial microenvironment can alter the production of endometrial cytokines, thus damaging endometrial function and leading to abnormal lymphocyte patterns in the endometrium. Together with altered secretion of paracrine factors, can reduce the receptivity of embryos causing female infertility.[3–5]

In 10-11% of women who undergo a "benign cause" hysterectomy[6] In 33.3-57.55% patients with infertility chronic endometritis is present. This is especially frequent in cases of repeated abortions and recurrent implantation failure after in vitro fertilization (IVF).[1,7]

Infection appears to be the basis of chronic endometritis. Some pathogen is found in up to 73.1% of patients[6].Common bacteria and Mycoplasma are the most frequently pathogens in chronic endometritis. Although female genital tuberculosis can cause chronic endometritis and infertility, it is anecdotal in industrialized countries and frequently is associated with predisposing factors.[5,6] The endometrial cultures were negative in about 31.7 % of the cases, probably due to the presence of nocultivable pathogen (like anaerobic bacterias or viruses) Different studies have shown that antibiotic therapy can restore normal endometrial histology, improving the rate of implantation.

Diagnosis

Diagnosis is a great challenge. It is frequently under diagnosed, cause of clinical manifestations, ultrasound and analytical markers are unspecified.[1,3,8,9]

While some patients are asymptomatic, others have dysfunctional uterine bleeding, pelvic algae, dyspareunia, and leucorrhea.[1,3] The most common symptoms is vaginal bleeding (reported in up to 94% of the patients).[10] Blood markers of infection, such as leukocytosis or C-reactive protein, do not appear elevated.[5]

Focal or diffuse periglandular hyperemia, increased thickness of the endometrium that appears white and with an irregular surface, micro-polyps (less than 1mm in size), pedunculated stromal edema are some of the diagnostic hysteroscopy signs. These lesions can be diffuse or cover most of the endometrial surface.[10] The relationship between endometrial polyps and chronic endometritis is unclear. In a recent study, an association between vascular changes in the functional layer of the endometrium and signs of chronic endometritis has been found, supporting the hypothesis that the vascular axis of the endometrial polyp represents an evolutionary stage of vasculopathy due to chronic endometritis (Figure 1) (Figure 2).[2]

While sensitivity of hysteroscopy is 98.4%, its specificity is 56.23%, the positive predictive value is 63.5%, and its negative predictive value is 97.52%.[11] For this reason, hysteroscopy is especially useful in diagnosis recognizing specific signs of chronic endometritis.[1,11,12] In these patients, two samples should be taken, one for a microbiological study and the other for a histopathological study. Cicinelli et al have obtained in their studies a diagnostic correlation of up to 93.4% based on hysteroscopic criteria during the follicular phase that suggest chronic endometritis.[2,7]

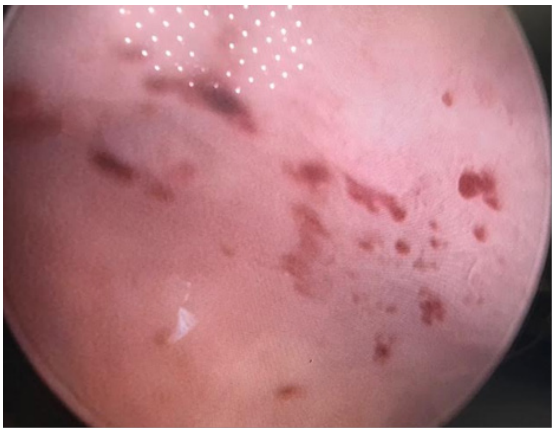

Figure 1 Tipical periglandular hyperhemia.

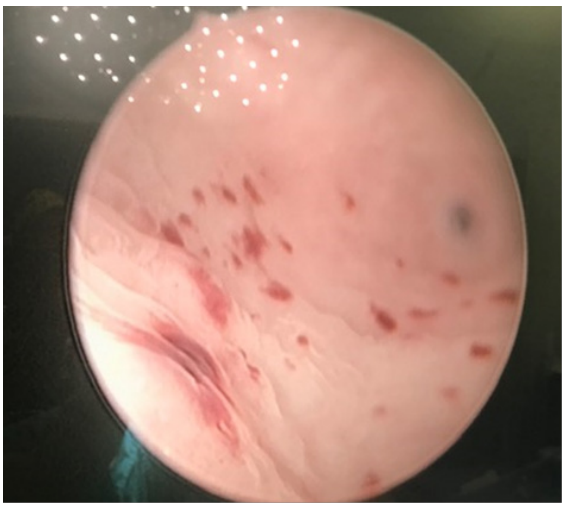

Figure 2 Tipical periglandular hyperhemia and irregular endometrial surface.

Bacterias are the most present infectious agent. It is possible found Streptococcus (27%), E. coli (11%), Enterococcus faecalis (14%) and Urea plasmaurealyticum (11%).[1,9] The presence of Chlamydia trachomatis is only 2.7%, and that of Neisseria gonorrhoeae is practically undetectable as a cause in chronic endometritis.[4,6]

From a histological point of view, it is common to find leukocytes in the endometrial lining, especially in the phase prior to menstruation. To increase diagnostic precision, immune histochemistry is recommended, in addition to conventional histology.[8] Hematoxylin and eosin study is less sensitive (13%) than the CD138 immuno histochemical study (56%)[6] to detect plasma cells in the stroma. endometrial. Syndecan 1, also known as CD138, is a transmembrane proteoglycan that is found on the surface of plasma cells and keratinocytes, but not on mononuclear cells, lymphocytes, or endometrial stromal cells. For this reason, its detection is used for diagnosis of chronic endometritis.[2,5,8,9]

Regarding the complementary ultrasonograpy, transvaginalsonography have no specific sign but free pelvic fluid on ultrasound appears to be associated with positive CD138 on endometrial collection.[8]

Treatement

Doxycycline 100mg each 12 hours for 14 days removes plasma cells CD138 from 70% to 96% of histological samples.[5,6]

Some studies recommends treat it according to the bacterial sample:

In Gram negative bacteria ciprofloxacin 500mg is used twice a day for 10 days. In the case of Gram positive bacteria amoxicillin 1gram plus clavulanic acid was prescribed twice a day for 8 days.

In case of negative bacterial sample but histological diagnosis of chronic endometritis, a treatment based on Ceftriaxone 250mg IM administered in a single dose together with Doxycycline 100mg orally twice a day for 14 days and Metronidazole 500mg orally twice a day for 14 days could be useful, according to Centers for Disease Control guidelines.

In case of persistent signs of chronic endometritis in subsequent hysteroscopy, the protocol could be repeated up to three times.[5,7]

Antibiotic treatment can attenuate the effect of chronic endometritis on infertility: in the study by Cicinelli et al, the pregnancy rate of the group with normalization of hysteroscopy after antibiotics was significantly higher than that of the group that did not respond to antibiotic therapy (61% vs. 10%). Moreover, McQueen et al study shows that the rate of live births per pregnancy in patients with chronic endometritis increased significantly to 56% after antibiotic treatment, compared to 7% before of treatment.[5,6]

Endometritis does not resolve in all cases after antibiotherapy. Several studies propose an hysteroscopy verification after antibiotherapy, modifying the treatment according to the clinical, hysteroscopy and histological findings.[4,5,7]

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Conflicts of interest

All authors declare that they have no competing interests.

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